Message

From: Michelle Deveau [michelle.deveau@hc-sc.gc.ca]
Sent: 7/30/2015 2:33:04 PM
To: Donohue, Joyce [Donohue.Joyce@epa.gov]
CC: Richard Carrier [richard.carrier@hc-sc.gc.ca]
Subject: RE: Peer review of Health Canada's draft Guideline Technical Documents for PFOS and PFOA
Attachments: PFOS Assessment June 22.docx; PFOA Assessment June 22.docx; Summit report FINAL.pdf; Summary of BMD modeling for endpoints in assessments.xlsx; Animal-to-human extrapolation calculations.xlsx

Hi Joyce,

Yes, an abbreviated review that focuses on the assessment approach would be very helpful to us, as getting EPA's input on that specific aspect would be the most important part of your review, it because you're in the final stages of your own review. Please don't worry about giving the detailed review that you'd normally give, if that saves you time; the focus on the approach itself would be perfect. We have more reviewers on these documents than we normally would, so there will be other people that will be able to focus on the other sections of the document.

I have attached the new charge questions and documents that we've sent to another reviewer who is doing a more abbreviated review on the dose-response assessment approach. The dose-response assessments in the attached documents are only 10-11 pages each (with ~5 of the pages devoted to the discussion of various interspecies extrapolation approaches, which is repeated between the documents, with only quantitative differences between the two). The appendices contain preliminary MOA analysis data as supplemental information; although this information drives some of the decisions made in the dose-response assessment, you don't have to worry about commenting on that if you don't have time. We have a couple of other reviewers with expertise on MOA analysis that will be reviewing that information, so it would be sufficient to state whether EPA's assessments will generally agree/disagree with the conclusions.

Please let me know if you think this approach is more feasible for you.

Thanks,
Michelle

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Peer review charge questions
Suggested questions to guide the review are listed below; however, please feel free to make comments on any additional topics that you see fit.

Selection of points of departure (PODs):

- Was the discussion sufficient to support the exclusion of immunological (PFOS) or developmental (PFOA) effects?
- Do you believe there is sufficient support provided for considering PFOA-induced liver weight increases and hepatocellular hypertrophy as PODs? If not, please provide additional data or guidance references that could be used to further support the decision, or identify whether you believe these effects to be adaptive.
    - If you consider the liver effects to be adaptive, please identify whether you believe cholesterol changes would be an appropriate POD for a health-based value

Animal-to-human extrapolation:

- Is the reasoning for using the PBPK model-derived CSAF values over other animal-to-human approaches sufficiently supported? If not, what further details would you suggest to include to strengthen the justification?
- Do you agree that this is the appropriate approach for the animal-to-human extrapolation? If not, please provide support for your preferred animal-to-human extrapolation approach.

- Is the reasoning for excluding the full use of the PBPK model to derive points of departure sufficiently supported?
-

Other questions:

- Are the correct uncertainty factors used? Are there any UFs that were not used that should be considered, or are there any UFs that were used that should be excluded, decreased, or increased?
- Do you agree with the conclusions of the mode of action analysis? (Detailed tables are included in Appendix A; the summary of the MOA analysis that is included in the draft GTD is provided in Appendix B)

Attached documents
The following documents have been attached to this email:

For your review:

- Draft dose-response assessment document for PFOS
- Draft dose-response assessment document for PFOA

As supplemental materials:

- Summit Toxicology report on animal-to-human extrapolation approaches
- Excel spreadsheet with benchmark dose modelling outputs for relevant endpoints
- Excel spreadsheet with calculations of the health-based values

If you require any further supplemental materials or articles referenced in the documents, please do not hesitate to contact Michelle Deveau.

Please note that this document has not yet undergone technical editing, so please do not worry about making this a focus of your revision (unless you identify an error that changes the scientific meaning of anything in the document).

If you have any questions or concerns, please do not hesitate to contact me.

Thanks,
Michelle

Michelle Deveau, M.Sc.(A), ROH
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(See attached file: PFOS Assessment June 22.docx)(See attached file: PFOA Assessment June 22.docx)(See attached file: Summit report FINAL.pdf)(See attached file: Summary of BMD modeling for endpoints in assessments.xlsx)(See attached file: Animal-to-human extrapolation calculations.xlsx)

"Donohue, Joyce" ---2015-07-30 09:55:49 AM---Dear Michelle: IRIS is not working on PFOS and PFOA. I am the person who is leading the health asses

From: "Donohue, Joyce" <Donohue.Joyce@epa.gov>
To: Michelle Deveau <michelle.deveau@hc-sc.gc.ca>
Cc: Richard Carrier <richard.carrier@hc-sc.gc.ca>
Date: 2015-07-30 09:55 AM
Subject: RE: Peer review of Health Canada's draft Guideline Technical Documents for PFOS and PFOA

Dear Michelle:

IRIS is not working on PFOS and PFOA. I am the person who is leading the health assessment effort for both chemicals at the moment.

I have started on the Manganese draft already and have a lot of comments before even getting to the Tox part. We are very interested in manganese since we added it to our CCL were hoping that we would be able to use your assessment for the next regulatory determination. Thus, I want to do a though review. We are using your selenium assessment for the current six-year review of regulations. I had reviewed that when it was being developed.

You can send me the shorter version of PFOA and PFOS, it you wish and I will look at them before Mn. I can certainly comment on your approach since it is their toxicokinetics that make them so complicated.

Joyce

From: Michelle Deveau [mailto:michelle.deveau@hc-sc.gc.ca]
Sent: Thursday, July 30, 2015 9:44 AM
To: Donohue, Joyce
Cc: Richard Carrier
Subject: RE: Peer review of Health Canada's draft Guideline Technical Documents for PFOS and PFOA

Hi Joyce,

I discussed this with Richard. Do you think it might be possible to do shorter reviews on both manganese and PFOA/PFOS, by focusing only on the Classification and Assessment Sections (i.e. selection of points of departure, dose-response analysis, and proposal of a health-based value)? I have a shorter version of PFOS and PFOA that we sent to another peer reviewer to keep their peer review shorter, so I could send that to you as well.

Alternatively, are there other people working on the PFOS & PFOA IRIS assessments that would be able to review our documents? It would be useful to have somebody who is working on that dose-response assessment to review and provide comments on our approach, even if it is not you.

Thanks,
Michelle

"Donohue, Joyce" ---2015-07-30 09:02:02 AM---Dear Michelle: I am quite up to date with PFOA and PFOS. Since I am currently working on finishing

From: "Donohue, Joyce" <Donohue.Joyce@epa.gov>
To: Michelle Deveau <michelle.deveau@hc-sc.gc.ca>
Date: 2015-07-30 09:02 AM
Subject: RE: Peer review of Health Canada's draft Guideline Technical Documents for PFOS and PFOA

Dear Michelle:

I am quite up to date with PFOA and PFOS. Since I am currently working on finishing the update to the PFOA and PFOA documents we peer reviewed last August. However, I have a complication because I will be at the DBP Gordon conference the second week of August and Richard asked me to complete a review of your manganese document by the 24th. Which is more important the PFCs or Mn? I have to balance your reviewing your Health Canada documents (Mn, PFOS and PFOA) with finishing ours.

Joyce

From: Michelle Deveau [mailto:michelle.deveau@hc-sc.gc.ca]
Sent: Wednesday, July 29, 2015 5:36 PM
To: Donohue, Joyce
Cc: Richard Carrier
Subject: Peer review of Health Canada's draft Guideline Technical Documents for PFOS and PFOA

Hello Joyce,

Thank you for agreeing to be a peer reviewer for the draft Guideline Technical Documents for the Guidelines for Canadian Drinking Water Quality for PFOS and PFOA. Based on your expertise and risk assessment experiences related to these compounds, we are looking forward to your insight on our draft documents. Below you will find some guidance and information related to your review.

Suggested deadline
In your previous discussions with Richard Carrier, a rough deadline of the end of August was given to you. However, we have recently become aware of new challenges in our scientific editing contracts, which will require longer time periods for the editing process. If your schedule allows you to complete the review earlier than the previously discussed date, this would be greatly appreciated. Moreover, if you are able to provide partial reviews early (e.g. if you have finished the review for one compound earlier than the other, or if you could provide your comments specific to Section 10, particularly if you're recommending changes to the health-based values), this would be greatly appreciated.

Peer review charge questions
Suggested questions to guide the review are listed below; however, please feel free to make comments on any additional topics that you see fit.

General questions:

- Was the document clear, transparent, and well written?
- Are you aware of any omitted studies that, if included, could affect the derivation of the Health-Based Values?

Selection of points of departure (PODs):

- Do you believe the correct PODs were selected for each compound? If not, please suggest your recommended POD(s), along with support for your selection. Please also suggest any additional PODs that you think should be considered for inclusion in the dose–response analyses.
- Was the discussion sufficient to support the exclusion of immunological (PFOS) or developmental (PFOA) effects?
- Do you believe there is sufficient support provided for considering PFOA-induced liver weight increases and hepatocellular hypertrophy as PODs? If not, please provide additional data or guidance references that could be used to further support the decision, or identify whether you believe these effects to be adaptive.
    - If you consider the liver effects to be adaptive, please identify whether you believe cholesterol changes would be an appropriate POD for a health-based value; if you do not, please suggest an alternative POD.

Animal-to-human extrapolation:

- Is the reasoning for using the PBPK model-derived CSAF values over other animal-to-human approaches sufficiently supported? If not, what further details would you suggest to include to strengthen the justification?

- Do you agree that this is the appropriate approach for the animal-to-human extrapolation? If not, please provide support for your preferred animal-to-human extrapolation approach.
- Is the reasoning for excluding the full use of the PBPK model to derive points of departure sufficiently supported?
-

Other questions:

- Are the correct uncertainty factors used? Are there any UFs that were not used that should be considered, or are there any UFs that were used that should be excluded, decreased, or increased?
- Do you agree with the conclusions of the mode of action analysis?

Attached documents
The following documents have been attached to this email:

For your review:

- Draft Guideline Technical Document for PFOS
- Draft Guideline Technical Document for PFOA

As supplemental materials:

- Summit Toxicology report on animal-to-human extrapolation approaches
- Excel spreadsheet with benchmark dose modelling outputs for relevant endpoints
- Excel spreadsheet with calculations of the health-based values
- Mode of action analysis tables

If you require any further supplemental materials or articles referenced in the documents, please do not hesitate to contact Michelle Deveau.

Focus of the review
We realize these documents are long, and that you might not have sufficient time to perform a thorough review of both documents. Our suggested areas for the focus of the document, from highest to lowest priority, are as follows:
1) Section 10 - Classification and Assessment (PFOS: pp. 41-52; PFOA: pp. 43-56)
2) Section 9.3 - Mode of action (PFOS: pp. 38-41; PFOA: pp. 40-43)
3) Sections 9.1 - Effects in humans (PFOS: pp. 16-23; PFOA: pp. 16-26) and 9.2 - Effects on experimental animals (PFOS: pp. 23-38 ; PFOA: pp. 26-40)
4) Section 8 - Kinetics and metabolism (Both documents: pp. 11-16)
5) Section 4 - Identity, use and sources in the environment (Both documents: pp. 4-7) and 5 - Exposure (Both documents: pp. 7-11)

Please note that this document has not yet undergone technical editing, so please do not worry about making this a focus of your revision (unless you identify an error that changes the scientific meaning of anything in the document).

If you have any questions or concerns, please do not hesitate to contact me.

Thanks,
Michelle

Michelle Deveau, M.Sc.(A), ROH
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(See attached file: PFOS GTD 2015-07 (for consultation) en.doc)(See attached file: PFOA GTD 2015-07 (for consultation).doc)(See attached file: Summit report FINAL.pdf)(See attached file: Summary of BMD modeling for endpoints in assessments.xlsx)(See attached file: Animal-to-human extrapolation calculations.xlsx)(See attached file: MOA Analysis Tables - PFOS.docx)(See attached file: MOA Analysis Tables - PFOA.docx)